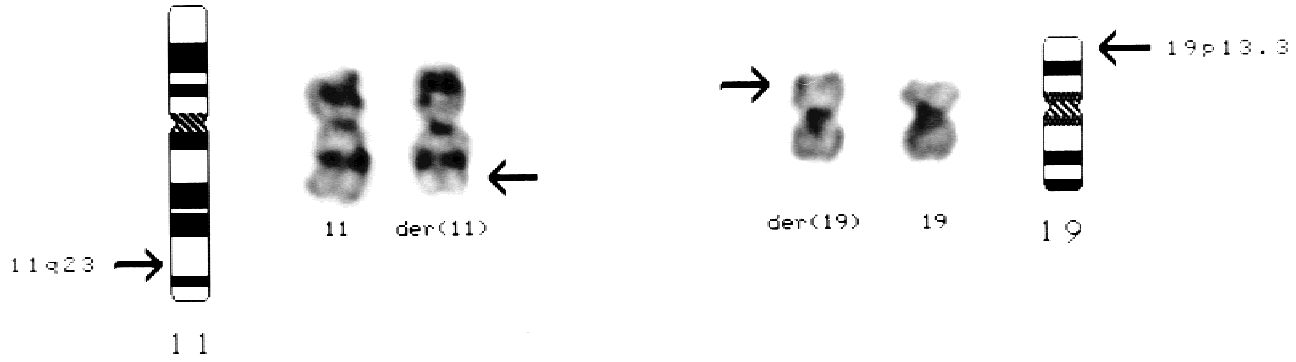

Fig. 1. Partial karyotype of the patient, showing t(11;19)(q23;p13.3), as revealed by G-banding technique. Breakpoints in the affected chromosomes are indicated by arrows.

M4 or M5 [1–3], with the M0 phenotype rarely observed. We now describe an adult patient with t-AML-M0 associated with t(11;19)(q23;p13.3) and *MLL* gene rearrangement that developed subsequent to epipodophyllotoxin therapy.

A 73-year-old Japanese man was diagnosed with unresectable stage IIIB small-cell carcinoma of the lung (SCLC) at the Kyushu Cancer Center in August 1992. The patient received four courses of EVAC-PE therapy (etoposide, vincristine, doxorubicin, cyclophosphamide, and cisplatin) and achieved partial remission. A low dose of etoposide was administered orally as maintenance therapy until December 1994 (cumulative dose of etoposide, 10,800 mg/m^2), at which time the SCLC remained in partial remission. In February 1995, the patient was admitted because of anemia, bleeding tendency, and pneumonia. Peripheral blood examination revealed Hb 8.2 g/dl, a platelet count of 26×10^9/l, and a white blood cell count of 3.2×10^9/l, with 51% blasts. Bone-marrow analysis detected 84.4% blasts, which were negative for both myeloperoxidase activity and staining with antibodies to myeloperoxidase. Mononuclear cells in the bone marrow were positive for HLA-DR, CD33, and CD11c, and negative for CD2, CD3, CD5, CD7, CD10, CD19, CD22, and CD34. Accordingly, the patient was diagnosed with t-AML-M0. Cytogenetic analysis showed a karyotype of 46,XY,t(11;19)(q23;p13.3) in all 20 bone-marrow cells examined (Fig. 1). Southern blot analysis demonstrated a rearrangement of the *MLL* gene (data not shown). Chemotherapy with behenoylcytosine arabinoside (BHAC), daunorubicin, and prednisolone was initiated, and the number of leukemic blasts subsequently decreased. In March 1995, the number of leukemic blasts again increased, and the patient was treated with granulocyte colony-stimulating factor combined with a low dose of subcutaneous cytosine arabinoside. Despite additional chemotherapy with BHAC, aclarubicin (ACR), and very low-dose ACR, remission was not achieved. The patient died of pulmonary infection 3 months after presentation. Autopsy showed that the SCLC was in a state of complete remission.

Only three cases of t-AML-M0 associated with epipodophyllotoxin treatment have previously been described [1,2]. Although chromosome rearrangements affecting band 11q23 were apparent in all 3 individuals, cytogenetic abnormalities involving this band are rarely associated with de novo AML-M0 [4].

t(11;19) translocations have been detected not only in childhood acute lymphoblastic leukemia and leukemias with monoblastic differentiation, but also in adult patients with AML expressing lymphoid-associated markers. Whereas t(11;19)(q23;p13.3) is predominant in younger individuals with lymphoid, biphenotypic, or congenital myeloid leukemia, t(11;19)(q23;p13.1) is frequently associated with both de novo and therapy-related AML, usually of the M4 or M5 phenotype, in patients of all ages [5]. Thus, translocations affecting region 19p13.3 tend to be associated with a more immature phenotype of leukemia than those involving 19p13.1.

We have described a rare case of adult t-AML-M0 that was associated with t(11;19)(q23;p13.3) and induced by treatment of SCLC with etoposide. The involvement of chromosome band 19p13.3 possibly contributed to the immature phenotype (M0) of the leukemia in this patient.

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Hypofibrinogenemia Induced by Prednisolone Therapy in a Patient With Chronic Lymphocytic Leukemia Complicated With Autoimmune Hemolytic Anemia

To the Editor: We report on the first instance of hypofibrinogenemia caused by sole administration of prednisolone (PSL).

In August 1992, a 54-year-old male developed antiglobulin test-positive autoimmune hemolytic anemia (AIHA) secondary to chronic lymphocytic leukemia (CLL) which had not been treated. He was given PSL (1 mg/kg/

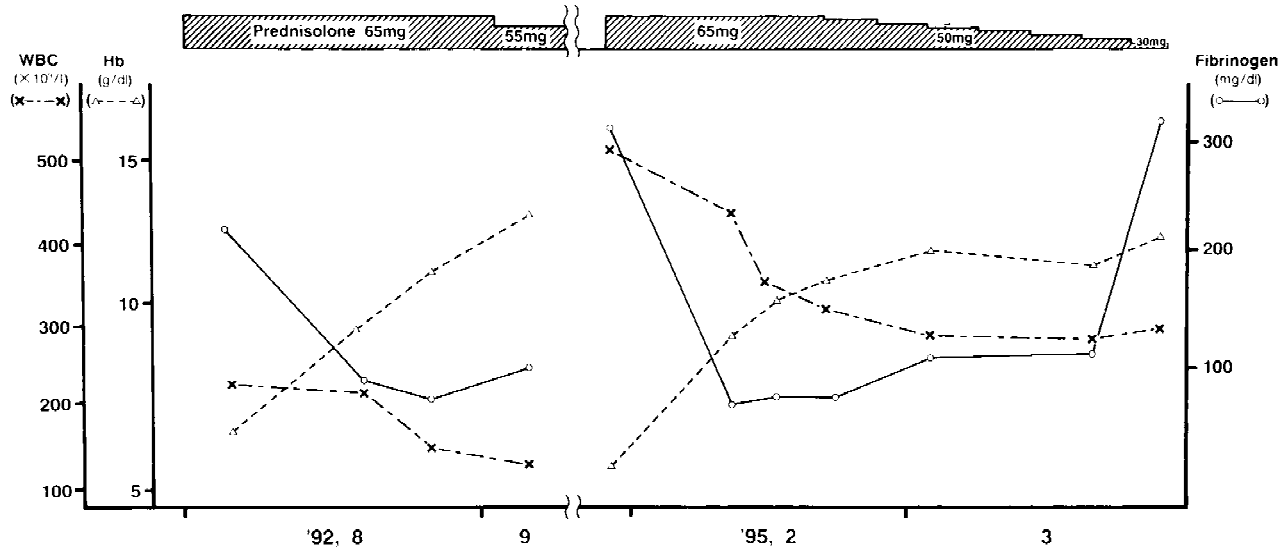

Fig. 1. Clinical course of patient. Shaded column at top shows dose of prednisolone. Dose of prednisolone was tapered from September 1992, and was 5 mg/day in January 1995 when the AIHA relapsed. Fibrinogen values determined by thrombin time method are shown.

day (65 mg/day)). After starting this therapy, the plasma fibrinogen level promptly decreased (Fig. 1). There was no clinical or laboratory evidence of disseminated intravascular coagulation (DIC) or liver disease. Further evaluation and follow-up study of the hypofibrinogenemia were not done at this time. In January 1995, when he received 5 mg of PSL, the AIHA relapsed. The laboratory findings were: white blood cells (WBC) 496.0 × 10^9/l (99.5% CLL cells), hemoglobin (Hb) 5.4 g/dl, reticulocytes 221.3 × 10^9/l, platelets 192 × 10^9/l, alanine aminotransferase 11 IU/l, lactate dehydrogenase 1,938 IU/l, indirect bilirubin 1.9 mg/dl, total protein 6.4 g/dl, albumin 4.3 g/dl, total cholesterol 171 mg/dl, haptoglobin 8.8 mg/dl (normal range, 41–318), and plasma fibrinogen 334 mg/dl (normal range, 200–400). DIC was not observed. He was given 65 mg/day of PSL again. Two weeks later, the plasma fibrinogen level decreased to 84 mg/dl. Both the thrombin time method and single radial immunodiffusion method showed similar low plasma fibrinogen values. Other coagulation studies were performed repeatedly, including the prothrombin time, activated partial thromboplastin time, hepaplastin time, plasma levels of factors VII and X, fibrin/fibrinogen degradation products, D-dimer, thrombin-anti-thrombin III complex, alpha 2-plasmin inhibitor-plasmin complex, fibrinopeptide A, and fibrin monomer complex; all showed normal values. After the anemia improved, the dose of PSL was gradually reduced. The plasma fibrinogen level did not return to normal until the dose of PSL was reduced to 30 mg/day (Fig. 1). There was no bleeding complication throughout the clinical course.

This case had no known causes of acquired hypofibrinogenemia (i.e., DIC, liver disease, or administration of drugs that impair protein synthesis in the liver, such as L-asparaginase, or that accelerate fibrinolysis), and the development of hypofibrinogenemia twice coincided with the use of PSL. The literature includes rare cases in which combination drug therapy containing a glucocorticoid induced hypofibrinogenemia [1–5]; most of these cases had lymphoid malignancies.

Therefore, it is highly likely that PSL induced the hypofibrinogenemia in this case. It is also possible that the malignant lymphoid cells played a role in the development of hypofibrinogenemia. In this case, it seems unlikely that the subclinical DIC or primary hyperfibrinogenolysis was induced by an unknown protease released from the CLL cells because all of the sensitive markers for DIC and primary fibrinogenolysis showed normal values. Fibrinogen is synthesized in the liver, is distributed mainly in the plasma, interstitial fluid, and lymph, and is catabolized by unknown mechanisms. Glucocorticoids may alter some step(s) in fibrinogen kinetics.

We suggest that glucocorticoids should be considered as a cause of acquired hypofibrinogenemia, especially in cases of lymphoid malignancy.

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Anti-Phospholipid-Antibody Syndrome Associated With Peripheral T-Cell Lymphoma

To the Editor: Peripheral T-cell lymphomas (PTCL) include heterogeneous diseases, among which only angioimmunoblastic T-cell lymphoma, angiocentric lymphoma, intestinal T-cell lymphoma, and adult T-cell lymphoma/leukemia can be considered distinct entities. The remainder, constituting